

REMARKS

Claims 1-56 are currently pending in this application. Claims 23-31 are withdrawn from consideration as allegedly drawn to unelected embodiments, and claims 1-22 and 32-56 are under consideration.

Independent claims 1, 5, and 19 and dependent claim 6 are currently amended, and dependent claims 10, 37, and 48 are currently amended for consistency with the amended independent claim from which they depend. Support for these amendments can be found in the specification and claims as originally filed, for example, at paragraphs [033], [036], [051], and [052] of the specification as filed, and the Examples. Accordingly, the claims have written description support.

FORMAL MATTERS

A. Withdrawn Objections and Rejections

Applicant acknowledges, with appreciation, that the Office has withdrawn the following rejections:

- The rejection of claims 1-5 and 7-22 as allegedly indefinite; and
- The rejection of claims 5, 6, and 19-22 as allegedly anticipated by Frengen in view of Chandler.

See Office Action at 2 (indicating that rejections not reiterated are withdrawn).

B. Information Disclosure Statement

Applicant thanks the Examiner for providing an initialed copy of the Form SB-08 that was filed April 3, 2002, indicating that the Office has considered all of the documents listed on that form.

REJECTIONS UNDER 35 U.S.C. § 112, ¶ 2

Claim 6 stands rejected as allegedly indefinite with respect to the terms “shortly” and “at the latest.” Office Action at 2-3. Applicant respectfully disagrees and traverses. However, solely to facilitate prosecution and without acquiescing to the Office's rationale, claim 6 is currently amended so as not to use the terms “shortly” and “at the latest.” Claim 6 as amended now recites in part that “time T2 is after addition of label L2, and time T1 occurs before 30% of time from addition of label L2 to time T2 has elapsed.” Applicant respectfully submits that claim 6 as amended is not indefinite and requests withdrawal of this rejection.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 1-4 and 7-15 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,739,042 to Frengen et al. (“Frogen”) in view of U.S. Patent No. 5,981,180 to Chandler et al. (“Chandler”). Office Action at 3. Frogen is cited by the Office for allegedly teaching a method involving incubating a sample with two independently determinable solid supported binding partners and a labeled ligand. The Office takes the position that these read on the analyte-A specific binding partners R1, R2, and R3 of claim 1. *Id.* at 3. The Office further alleges that Frogen teaches using “a substantial excess of the second form of solid-supported binding member (R3).” *Id.* at 10. The Office also alleges that Frogen teaches the use of flow cytometry and that Chandler establishes that flow cytometry inherently involves detecting particles at different time intervals. *Id.* at 4.

Applicant respectfully disagrees and traverses. Applicant previously argued that Frogen does not provide guidance regarding the selection of analyte binding partners

based on saturation of their analyte binding sites, while the instant claims recite that “saturation of analyte A-binding sites of the binding partner R2 requires a) a higher analyte A concentration, b) a longer incubation, or c) a higher analyte A concentration and a longer incubation, than does saturation of analyte A-binding sites of the binding partner R3.” Furthermore, Applicant argued that Frengen teaches determining measurement signals at the same time, but the instant claims recite “determining an L1-dependent measurement signal at time T1 and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal at time T2, wherein time T1 and time T2 are different.” In particular, in Frengen’s flow cytometry method, light scattering and fluorescence signals associated with individual particles are detected simultaneously.

However, the Office alleges that Frengen teaches a substantial excess of the second form of solid-supported binding member, which allegedly reads on R3, that the first form of binding partner, which allegedly reads on R2, is supplied in a low amount, and that the member corresponding to R2 requires a longer time than R3 for saturation, for reasons stated in Frengen. Office Action at 10-11. The Office further alleges that Chandler establishes that Frengen teaches flow cytometry methods in which measurements are made of multiple particles and that these measurements do not occur simultaneously, thereby meeting the above limitation. *Id.* at 11.

Solely to facilitate prosecution and without acquiescing to the Office’s rationale, independent claim 1 is currently amended to further distinguish it from the cited art. The other claims to which this rejection applies, claims 2-4 and 7-15, all depend directly or indirectly from claim 1. Claim 1 as amended recites in part that “either: (1) the solid phase with which the analyte A-specific binding partner R1 is associated is chosen from

a vessel, tube, microtitration plate, filter paper, and chromatography paper, or (2) the labels L1 and L2 are chosen from enzymes, fluorescent compounds, chemiluminescent compounds, and radioactive compounds.”

“A claim is anticipated only if *each and every element* as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” M.P.E.P. § 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987)) (emphasis added). Further, a rejection under Section 102 is proper only when the claimed subject matter is *identically* described or disclosed in the prior art. *In re Arkley*, 455 F.2d 586, 587, 172 U.S.P.Q. 524, 526 (C.C.P.A. 1972) (emphasis added). The identical invention must be described in as complete detail as is contained in, and must be arranged as required by, the claim. M.P.E.P. § 2131.

Frengen does not teach a method in which “the solid phase with which the analyte A-specific binding partner R1 is associated is chosen from a vessel, tube, microtitration plate, filter paper, and chromatography paper” that also meets all other limitations of the claims. The methods of Frengen do not teach performing an assay with such a solid phase in which the above limitation is met, at least because flow cytometry is not compatible with complexes in which a component is associated with a solid phase chosen from a vessel, tube, microtitration plate, filter paper, and chromatography paper, because the recited types of solid phase would not allow analyte complexes to flow through the examination zone of a flow cytometer in single file.

None of a vessel, tube, microtitration plate, filter paper, and chromatography paper would fit in the examination zone of a flow cytometer, and furthermore, attachment to any of these types of solid phases would prevent the materials to be analyzed from being arranged in single file. Applicant respectfully points out that the Office cites Chandler and specifically takes the position that “flow cytometry **requires** a fluid suspension of particles in a flow down a stream **in single file.**” Office Action at 4 (emphasis added). Applicant further points out that Frengen contains only a single example, which was performed via flow cytometry, and the solid phases were beads. See Frengen at col. 9, I. 49 - col. 11, I. 6, especially col. 9, II. 54-56.

Frenge also does not teach a method in which “the labels L1 and L2 are chosen from enzymes, fluorescent compounds, chemiluminescent compounds, and radioactive compounds” that also meets all other limitations of the claims. Frengen does not teach or suggest using two analyte specific binding partners labeled in this way, because the methods of Frengen involve two independently determinable forms of solid supported binding partner (i.e., two distinguishable types of beads) and one labeled ligand; in order to apply Frengen as a reference, the Office has taken the position that Frengen teaches solid supports that allegedly read on the L1 and L2 labels of the previous version of the instant claims. See, e.g., Office Action at 3. Solid supports are not enzymes, fluorescent compounds, chemiluminescent compounds, or radioactive compounds. Therefore, Frengen does not describe an assay in which the labels L1 and L2 are both of the recited types that also meets all the other claim limitations.

Thus, Frengen does not describe a method in which “either: (1) the solid phase with which the analyte A-specific binding partner R1 is associated is chosen from a

vessel, tube, microtitration plate, filter paper, and chromatography paper, or (2) the labels L1 and L2 are chosen from enzymes, fluorescent compounds, chemiluminescent compounds, and radioactive compounds” that also meets all other limitations of the claims, and Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 102(b).

REJECTIONS UNDER 35 U.S.C. § 103

A. Claims 5, 6, 19-22, 32-42, and 46-53

Claims 5, 6, 19-22, 32-42, and 46-53 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Frengen in view of Bayer et al., “The Avidin-Biotin System,” *Immunoassay* pp. 237-267 (1996) (“Bayer”). Office Action at 5-6. Bayer is cited for allegedly teaching the use of avidin-biotin binding in immunoassays, including to mediate between a primary antibody and a label. *Id.* at 6.

Applicant respectfully disagrees and traverses. However, like claim 1, independent claims 5 and 19 are currently amended to recite that “either: (1) the solid phase with which the analyte A-specific binding partner R1 is associated is chosen from a vessel, tube, microtitration plate, filter paper, and chromatography paper, or (2) the labels L1 and L2 are chosen from enzymes, fluorescent compounds, chemiluminescent compounds, and radioactive compounds.” Additionally, claims 37 and 48 now require that “the labels L1 and L2 are chosen from enzymes, fluorescent compounds, chemiluminescent compounds, and radioactive compounds.” As discussed above, these limitations are not taught by Frengen.

Applicant respectfully submits that Bayer does not remedy these deficiencies. This is because Frengen’s use of two forms of solid-supported binding partner and of

flow cytometry are fundamental to Frengen's disclosure and Bayer, concerning the use of avidin-biotin binding, would not lead one of ordinary skill to modify fundamental features of Frengen. Frengen states that "according to one aspect of the present invention there is provided a method . . . comprising reacting a sample with two independently determinable forms of solid-supported binding partner" Frengen at col. 3, ll. 56-60. This is the only "aspect" that Frengen discloses; therefore, Frengen's methods necessarily comprise "reacting a sample with two independently determinable forms of solid-supported binding partner."

Nor would one of ordinary skill, in view of Bayer, modify the method of Frengen so as to choose the solid phase with which the analyte A-specific binding partner R1 is associated from a vessel, tube, microtitration plate, filter paper, and chromatography paper. This is because Frengen teaches away from such a modification. Frengen teaches that "separation of the bound analyte and label and associated washing steps are inherently time-consuming and labor-intensive. It is known, however, that this problem may in principle be avoided in the case of particle-based assays if the particles are analysed by means of flow cytometry." *Id.* at col. 1, l. 64 - col. 2, l. 2. As Frengen necessarily involves the use of two independently determinable forms of solid-supported binding partner, referred to here as particles, a person of ordinary skill would not modify Frengen not to use flow cytometry, and so said person would not choose a solid phase with which the analyte A-specific binding partner R1 is associated from a vessel, tube, microtitration plate, filter paper, and chromatography paper. Thus, the claims are not obvious over Frengen in view of Bayer, and Applicant respectfully requests withdrawal of this rejection.

B. Claims 16 and 17

Claims 16 and 17 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Frengen in view of Buranda T. et al., "Peptides, Antibodies, and FRET on Beads in Flow Cytometry: A Model System Using Fluoresceinated and Biotinylated β -Endorphin," *Cytometry*, 37:21-31 (1999) ("Buranda"). Office Action at 7. Buranda is cited for allegedly teaching the use of fluorescence resonance energy transfer in flow cytometric determinations of binding constants. *Id.*

Applicant respectfully disagrees and traverses. However, claims 16 and 17 depend from claim 1 directly or indirectly, and claim 1 has been amended as discussed above. Furthermore, Applicant respectfully submits that one of ordinary skill would not modify fundamental aspects of Frengen in view of Buranda for the same reasons as discussed above with respect to the rejection over Frengen in view of Bayer. Thus, the claims are not obvious over Frengen in view of Buranda, and Applicant respectfully requests withdrawal of this rejection.

C. Claims 16 and 18

Claims 16 and 18 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Frengen in view of Ullman E.F. et al., "Luminescent Oxygen Channeling Immunoassay: Measurement of Particle Binding Kinetics by Chemiluminescence," *PNAS*, 91:5426-30 (1994) ("Ullman"). Office Action at 7-8. Ullman is cited for allegedly teaching particles comprising photosensitizers and chemiluminescent compounds utilized in luminescent immunoassays. *Id.*

Applicant respectfully disagrees and traverses. However, claims 16 and 18 depend from claim 1 directly or indirectly, and claim 1 has been amended as discussed

above. Furthermore, Applicant respectfully submits that one of ordinary skill would not modify fundamental aspects of Frengen in view of Ullman for the same reasons as discussed above with respect to the rejection over Frengen in view of Bayer. Thus, the claims are not obvious over Frengen in view of Ullman, and Applicant respectfully requests withdrawal of this rejection.

D. Claims 43, 44, 54, and 55

Claims 43, 44, 54, and 55 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Frengen in view of Bayer and Buranda. Office Action at 8.

Applicant respectfully disagrees and traverses. However, these claims depend from claims 5 or 19 directly or indirectly, and claims 5 and 19 have been amended as discussed above. Furthermore, Applicant respectfully submits that one of ordinary skill would not modify fundamental aspects of Frengen in view of Bayer and Buranda for the same reasons as discussed above with respect to the rejection over Frengen in view of Bayer. Thus, the claims are not obvious over Frengen in view of Bayer and Buranda, and Applicant respectfully requests withdrawal of this rejection.

E. Claims 45 and 56

Claims 45 and 56 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Frengen in view of Bayer, Buranda, and Ullman. Office Action at 9.

Applicant respectfully disagrees and traverses. However, claims 45 and 56 depend indirectly from claims 5 and 19, respectively, which have been amended as discussed above. Furthermore, Applicant respectfully submits that one of ordinary skill would not modify fundamental aspects of Frengen in view of Bayer, Buranda, and Ullman for the same reasons as discussed above with respect to the rejection over

Frengen in view of Bayer. Thus, the claims are not obvious over Frengen in view of Bayer, Buranda, and Ullman, and Applicant respectfully requests withdrawal of this rejection.

CONCLUSION

Applicant respectfully requests that this Amendment and Reply under 37 C.F.R. § 1.116 be entered by the Examiner, placing the claims in condition for allowance. Applicant respectfully points out that the final action by the Examiner presented some new arguments as to the application of the art against Applicant's invention. It is respectfully submitted that the entering of the Amendment would allow the Applicant to reply to the final rejections and place the application in condition for allowance.

Applicant also submits that the entry of the amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.


In view of the foregoing remarks, Applicant submits that this claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicant therefore requests the entry of this Amendment, the Examiner's reconsideration of the application, and the timely allowance of the pending claims. If the Examiner believes that a telephone conversation would help to resolve any remaining issues, he is respectfully invited to contact the undersigned.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

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